

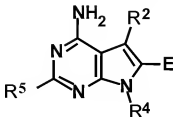
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. - 2. (canceled)

3. (currently amended) A compound having the formula (IA):



(IA)

in which

R² is hydrogen or a group having the formula (CH₂)_bR^b wherein *b* is 0 or an integer from 1 to 3 and R^b is an aromatic, heterocyclic or cyclical aliphatic group optionally substituted with one or more groups selected from lower alkyl, halogen, substituted alkyl, nitro, alkoxy, phenoxy, sulfonamido, carboxylic ester, or carboxamide;

R⁴ is an aliphatic, aromatic, or heterocyclic group optionally substituted with one or more polar groups, which polar group may be protected or unprotected;

R⁵ is hydrogen or an alkyl- or aryl-substituted ether, thioether, or amine; and

~~E is an electrophilic group capable of forming a covalent bond with a cysteine residue within the ATP-binding site of a kinase comprises a carbonyl group, an epoxide, or an olefin conjugated to an electron withdrawing group;~~

provided that the compound is not a compound in which, R² is 4-phenoxyphenyl, E is cyano, R⁴ is cyclopentyl, and R⁵ is hydrogen.

4. (canceled)

5. (currently amended) A compound according to claim ~~2~~ or 3 in which R^2 is hydrogen.

6. (currently amended) A compound according to claim ~~2~~ or 3 in which R^2 is a group having the formula $(CH_2)_bR^b$.

7. (original) A compound according to claim 6 in which b is 0.

8. (original) A compound according to claim 7 in which R^2 is an optionally substituted phenyl group.

9. (canceled)

10. (currently amended) A compound according to claim ~~9~~ 3 in which E comprises an olefin conjugated to a carbonyl, nitro, cyano, carboxyl, carboxamide, sulfoxide, sulfonyl, sulfonamide, or sulfonate group.

11. (currently amended) A compound according to ~~claims 2 or~~ claim 3 in which E comprises a carbonyl group.

12. (currently amended) A compound according to claim 11 in which ~~the carbonyl group~~ E has the formula $-C(O)(CH_2)_nR$ in which R is a halogen and n is 0 or an integer from 1 to 6.

13. (original) A compound according to claim 12 in which n is 0.

14. (original) A compound according to claim 12 in which n is 1.

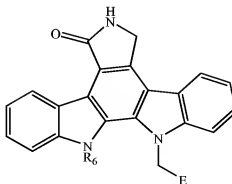
15. (currently amended) A compound according to claim 11 in which ~~the carbonyl group~~ E has the formula $-(CH_2)_mC(O)R$ in which m is 0 or an integer from 1 to 6 and R is a halogen.

16. (original) A compound according to claim 15 in which m is 0.

17. (original) A compound according to claim 15 in which m is 1.

18. (original) A compound according to any of claims 12-17 in which R is chloro.

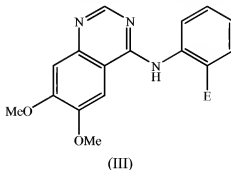
19. (original) A compound according to any of claims 12-17 in which R is fluoro.
20. (currently amended) A compound according to claim 11 in which the ~~carbonyl group~~ E comprises an olefinically unsaturated ketone.
21. (currently amended) A compound according to claim 20 in which the ~~carbonyl group~~ E is $-C(O)CH=CH_2$.
22. (currently amended) A compound according to ~~claims 2 or~~ claim 3 in which E is an olefin carboxylate having the formula $CH=CHC(O)OR'$ where R' is an optionally substituted aliphatic, aromatic, or heterocyclic moiety.
23. (original) A compound according to claim 22 in which R' is methyl.
24. (currently amended) A compound according to ~~claims 2 or~~ claim 3 in which E is an olefin carboxamide having the formula $-CH=C(O)NR''$ where R'' and R''' are optionally substituted aliphatic, aromatic, or heterocyclic moieties.
25. (currently amended) A compound according to ~~claims 2 or~~ claim 3 in which E comprises an epoxide.
26. (withdrawn) A compound having the formula (II):



(II)

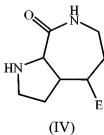
in which R₆ is hydrogen or an optionally substituted aliphatic, aromatic or heterocyclic group and E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

27. (withdrawn) A compound having the formula (III):



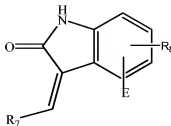
in which E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

28. (withdrawn) A compound having the formula (IV):



in which E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

29. (withdrawn) A compound having the formula (V):



(V)

in which R_7 is a group having the formula $(CH_2)_bR^b$ wherein b is 0 or an integer from 1 to 3 and R^b is an aromatic, heterocyclic or cyclical aliphatic group; R_8 is hydrogen or one or more substituents that do not affect the kinase-inhibiting properties of the said compounds, and E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

30. (withdrawn) A compound according to any of claims 26-29 in which E comprises a carbonyl, an epoxide, or an olefin conjugated to an electron withdrawing group.

31. (withdrawn) A compound according to any of claims 26-29 in which E comprises an olefin conjugated to a carbonyl, nitro, cyano, carboxyl, carboxamide, sulfoxide, sulfonyl, sulfonamide, or sulfonate group.

32. (withdrawn) A compound according to any of claims 26-29 in which E comprises a carbonyl group.

33. (withdrawn) A compound according to claim 32 in which the carbonyl group has the formula $-C(O)(CH_2)_nR$ in which R is a halogen and n is 0 or an integer from 1 to 6.

34. (withdrawn) A compound according to claim 33 in which n is 0.

35. (withdrawn) A compound according to claim 33 in which n is 1.

36. (withdrawn) A compound according to claim 32 in which the carbonyl group has the formula $-(CH_2)_mC(O)R$ in which m is 0 or an integer from 1 to 6 and R is a halogen.

37. (withdrawn) A compound according to claim 36 in which m is 0.

38. (withdrawn) A compound according to claim 36 in which m is 1.

39. (withdrawn) A compound according to any of claims 33-38 in which R is chloro.

40. (withdrawn) A compound according to any of claims 33-38 in which R is fluoro.

41. (withdrawn) A compound according to claim 32 in which the carbonyl group comprises an olefinically unsaturated ketone.

42. (withdrawn) A compound according to claim 41 in which the carbonyl group is -C(O)CH=CH_2 .

43. (withdrawn) A compound according to any of claims 26-29 in which E is an olefin carboxylate having the formula CH=CHC(O)OR' where R' is an optionally substituted aliphatic, aromatic, or heterocyclic moiety.

44. (withdrawn) A compound according to claim 43 in which R' is methyl.

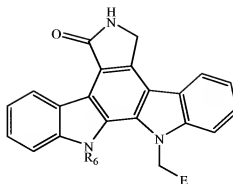
45. (withdrawn) A compound according to any of claims 26-29 in which E is an olefin carboxamide having the formula -CH=C(O)NR''R'' where R'' and R''' are optionally substituted aliphatic, aromatic, or heterocyclic moieties.

46. (withdrawn) A compound according to any of claims 26-29 in which E comprises an epoxide.

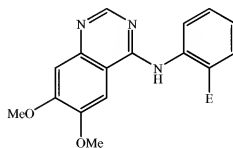
47. (currently amended) A method of inhibiting a protein kinase that has one or more cysteine residues within its ATP binding site, comprising contacting the kinase with an inhibitory-effective amount of a compound according to claim 3 ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase.~~

48. - 49. (canceled)

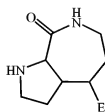
50. (withdrawn) A method of inhibiting a protein kinase that has one or more cysteine residues within its ATP binding site, comprising contacting the kinase with an inhibitory-effective amount of a compound having the formula (II), (III), (IV) or (V):



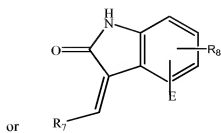
(II)



(III)



(IV)



(V)

in which R_6 is an optionally substituted aliphatic, aromatic or heterocyclic group; R_7 is a group having the formula $(CH_2)_bR^b$ wherein b is 0 or an integer from 1 to 3 and R^b is an optionally substituted aromatic, heterocyclic or cyclical aliphatic group;; R_8 is hydrogen or one or more substituents that do not affect the kinase-inhibiting properties of the said compounds, and E represents an electrophilic group that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase.

51. (currently amended) A method of imparting to a protein kinase the capability of being inhibited by a compound ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of reacting with a cysteine residue within the ATP binding site of a kinase according to claim 3,~~ comprising replacing an amino acid residue other than a cysteine residue within the ATP binding site of the protein kinase with a cysteine residue.

52. (currently amended) A method of imparting to a protein kinase the capability of being inhibited by a compound ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase according to claim 3,~~ comprising replacing a methionine, leucine, isoleucine, lysine, arginine, tryptophan, glutamine, asparagine, proline, tyrosine, histidine, glutamic acid, aspartic acid, valine, or phenylalanine residue in the gatekeeper position of the ATP binding site with a smaller residue.

53. (currently amended) A method for inhibiting the morphological transformation of a cell in which such a kinase is expressed comprising contacting the cell or the kinase with an inhibitory-effective amount of a compound ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom; and an electrophilic substituent that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase according to claim 3.~~

54. (currently amended) A method for inhibiting the proliferation of a tumor cell comprising contacting the cell with an inhibitory-effective amount of a compound ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase according to claim 3.~~

55. - 56. (canceled)

57. (withdrawn) A method according to claim 54 in which the compound is a compound according to any of claims 26-29.

58. (original) A method according to claim 54 in which the cell is contacted with an inhibitory-effective amount of a plurality of such compounds.

59. (currently amended) An array for testing for inhibition of protein kinase activity comprising one or a plurality of compounds ~~having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase~~ according to claim 3.

60. (currently amended) A therapeutic composition comprising (a) a kinase inhibitory-effective amount of a composition according to ~~any of claims 1-46~~ claim 3 and a pharmaceutically acceptable carrier.

61. (currently amended) A composition for inhibiting kinase activity comprising an effective inhibitory amount of a compound according to ~~any of claims 1-46~~ claim 3.

62. (original) A composition according to claim 62 for inhibiting activity of a kinase selected from the group consisting of Rsk1,2,3,4, Msk1-2, Plk1-3, MEKK1, and Nck2.